UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,810	04/12/2004	Jennifer Lynne Reed	IL500US	5467

36577 7590 05/01/2007
JOHNATHAN KLEIN-EVANS
ONE MEDIMMUNE WAY
GAITHERSBURG, MD 20878

EXAMINER	
CHANDRA, GYAN	
ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
05/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,810	REED, JENNIFER LYNNE	
	Examiner	Art Unit	
	Gyan Chandra	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *11,14,16,17,22,25,26,28 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12,13,15,18-21,23,24,27,29-30 and 32-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Re: Reed, J.L.

Date of Priority: 4/11/2003 (US 60/60/462,307)

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-3, 6-7, 9-14, 23-26, and 29-31 and election of species (influenza virus) in the reply filed on 2/22/2007 is acknowledged. The traversal is on the ground(s) that examining Group I and II comprise a common method step of "administering ...an effective amount of an IL-9 antagonist." Applicants argue (page 3 of Response) that search results from Group II would find relevant arts for Group I and therefore searching for Groups I and II would not be a serious search burden. This is found persuasive and Groups I and II are being examined together. Applicant did not traverse the election of species.

The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, And/Or Claims

Claims 1-36 are pending.

Claims 11, 14, 16, 17, 22, 25, 26, 28 and 31 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1-10, 12-13, 15, 18-21, 23, 24, 27, 29-30 and 32-36 are being examined to the extent they read on the elected species (i.e., influenza virus).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-10, 15, 18-21, 23, 24, 27, 29-30 and 32-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administering an IL-9 antagonist to treat or ameliorate a respiratory infection, wheezing, asthma or an allergy in human subject, does not reasonably provide enablement for preventing or managing a respiratory infection, wheezing, asthma or an allergy in human subject a human child or preterm infant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to which the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face,

contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986).

Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed..

The instant disclosure fails to meet the enablement requirement for the following reasons:

Claims 1, 3-10, 15, 18-21, 23, 24, 27, 29-30 and 32-36 are drawn to a method of managing, preventing, treating or ameliorating a respiratory infection, wheezing, asthma or an allergy in a human subject, a human child or a human pre-term infant comprising administering an effective amount of (i) IL-9 antagonist, or (ii) IL-9 antagonist and at least one other asthma therapy that is not IL-9 antagonist.

The amount of direction and guidance present and the presence or absence of working examples: With regards to the prevention of asthma, wheezing, respiratory infection or an allergy in a human subject, a human child or a human pre-term infant comprising administering an effective amount of (i) IL-9 antagonist or (ii) IL-9 antagonist and at least one other asthma therapy that is not IL-9 antagonist, the specification does

not disclose sufficient guidance or objective evidence that such antagonists or in a combination with another asthma therapy would predictably prevent respiratory infection, wheezing, asthma or even an allergy in a human subject, a human child or a human pre-term infant. The specification on page 40 defines that the term "managing" or "manage" encompasses preventing the progression or worsening of the disease, and the specification on page 41 defines the term "preventing" as the prevention of the recurrence, onset, development of one or more symptoms of a respiratory condition in a subject. The specification, on pages 218-219, teaches that IL-9 increases airway hyperresponsiveness in the mouse strain BLB/c. Although, it is possible to inhibit or reduce the symptoms related with respiratory infection, wheezing, asthma or even an allergy in a human subject to some extent, the prevention or management (as defined in the instant specification) of respiratory infection, wheezing, asthma or even an allergy is highly unpredictable.

The state of the prior art and the predictability or lack thereof in the art:

The majority of studies suggest that the essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in advance clinical settings and link those results with subsequent histological confirmation of the presence or absence of disease. Cheng et al (Am. J. Resp. Crit. Care Med. 166: 409-416, 2002) teach that IL-9 increases IgE level, airway inflammation, lung eosinophilia, mast cell hyperplasia and bronchial hyperresponsiveness (page 409, right column). Levitt et al (US Patent Nos. 6,261,559 and 6,645,492) teach that IL-9 plays role in a pathogenesis of atopic allergy, including bronchial hyperresponsiveness,

asthma, and related disorders (column 8). Levitt et al teach a method of alleviating asthma by administering an IL-9 antagonist (claims 1-11). Hennet et al (J. Immunol.149: 932-939, 1992) teach that many cytokines and leukotrienes B4 are secreted in the lungs in response to infections e.g., influenza-induced pneumonia (page 932). David P. Skoner (Pediatrics 109: 381-392, 2002) teaches treating asthma and related symptoms administering various PDE inhibitors, ICS (inhaled corticosteroids), leukotriene receptor antagonists such as Zafirlukast, Montelukast) or long acting β2 agonists to children (pages 386-389). One skilled in the art also uses a combination therapy where more than one compound is administered for treating asthma and other respiratory infections. But the art does not teach preventing asthma, wheezing, respiratory infection or an allergy in a human subject, a human child or a human pre-term infant by administering an IL-9 antagonist.

The breadth of the claims and the quantity of experimentation needed:

The specification is devoid of any models or experimental analysis that reasonably suggests that the claimed method would predictably either prevent or manage asthma, wheezing, respiratory infection or an allergy in a human subject, a human child or a human pre-term infant. This, combined with the state of the art of preventing or managing asthma, wheezing, respiratory infection or an allergy in a human subject, a human child or a human pre-term infant, suggests that undue experimentation would be required to practice the invention as broadly claimed.

Claims 2 and 12-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 2 and 12-13 are drawn to a method of preventing the development, onset or progression of one or more asthma-like symptom or asthma in a human child that previously had respiratory infection comprising administering an effective amount of (i) IL-9 antagonist.

With regards to preventing the development, onset or progression of one or more asthma-like symptom or asthma in a human child that previously had respiratory infection comprising administering an effective amount of (i) IL-9 antagonist, the specification does not disclose sufficient guidance or objective evidence that such antagonists would predictably prevent the development, onset or progression of one or more asthma-like symptom or asthma in a human child that previously had respiratory infection. The specification on page 41 defines the term "preventing" as the prevention of the recurrence, onset, development of one or more symptoms of a respiratory condition in a subject. Although, it is possible to inhibit or reduce the symptoms related with respiratory infection, wheezing, asthma or even an allergy in a human subject to some extent as taught by Levitt et al (US Patent Nos. 6,261,559 and 6,645,492), the prevention (as defined in the instant specification) of the development, onset or

progression of one or more asthma-like symptom or asthma in a human child that previously had respiratory infection is highly unpredictable.

The specification, on pages 218-219, teaches that IL-9 increases airway hyperresponsiveness in the mouse strain BLB/c. The specification is devoid of any models or experimental analysis that reasonably suggests that the claimed method would predictably prevent the development, onset or progression of one or more asthma-like symptom or asthma in a human child that previously had respiratory infection in a human child. This, combined with the state of the art of preventing the development, onset or progression of one or more asthma-like symptom or asthma in a human child that previously had respiratory infection, suggests that undue experimentation would be required to practice the invention as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless –**
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6-7, 23, and 36 is rejected under 35 U.S.C. 102(b) as being anticipated by Levitt et al. (US Patent No. 6,261,559, published on 7/17/2001).

Claims 1, 6-7, 23, and 36 are broadly drawn to a method of treating or ameliorating a respiratory infection or a symptom thereof in a human subject suffering therefrom, said method comprising administering an effective amount of an IL-9

antagonist to said human subject, wherein said antagonist is an antibody that specifically binds to an IL-9 receptor, wherein IL-9 antagonist is an antibody that immuno-specifically binds to an IL-9 polypeptide and wherein said IL-9 antagonist is administered orally or intranasally (claim 23 and 36).

Levitt et al teach that IL-9 plays role in a pathogenesis of atopic allergy, including bronchial hyperresponsiveness, asthma, and related disorders (column 8). Levitt et al teach a method of alleviating asthma by administering an IL-9 antagonist to a patient (claims 1-5). Levitt et al teach administering an antibody that specifically binds IL-9/IL-9 receptor can optionally provide complete protection from antigen induced airway hyperresponsiveness and inflammation (column 10, lines 51+, col., lines 14+, claim 10). Levitt et al teach administering an antibody by one or more of routes selected from the group consisting of intravenous, intra-peritoneal, inhalation, intramuscular, subcutaneous or oral (claim 6, 8-9).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-5, 8, 15, 18-21, 27 and 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levitt et al. (2001) in view of Skoner (Pediatrics 109: 381-392, 2002).

Claims 3-5, 8, 15, 18-21, 24, 27 and 32-35 are broadly drawn to a method of treating or ameliorating a respiratory infection or a symptom thereof in a human subject suffering therefrom, said method comprising administering an effective amount of an IL-9 antagonist and an effective amount of one other asthma or allergy therapy to said human subject (claims 4-5, 20-21), wherein subject is a human child or pre-term infant (claims 3, 24, 27, 32-35), wherein further administering comprises an effective amount of one other therapy (i.e. a leukotriene modifier montelukast such as zafirlukast, pranleukast or zileuton) (claims 8, 18-19), and wherein the said therapy is an anti-inflammatory agent (claim 15).

The teachings of Levitt are summarized as set forth supra. Leavitt et al teach combining more than one IL-9 antagonists together for a better result but Levitt et al do not teach combing another asthma therapy that is not IL-9 antagonist. Levitt et al also do not teach administering IL-9 antagonist to a subject wherein said subject is a child or pre-term infant.

Skoner teaches treating childhood asthma and related symptoms administering various PDE inhibitors, ICS (inhaled corticosteroids), leukotriene receptor antagonists such as Zafirlukast, Montelukast) or long acting β2 agonists to children (pages 386-389) (claims 3, 27, 32-35). Skoner teaches administering ICS and one more asthma therapy montelukast significantly increases pulmonary functions and symptoms (page 387, left column) (claims 8, and 18-19). Skoner teaches that the LTRAs reduce inflammation associated with asthma, which is an anti-inflammatory property of an agent (claim 15). Skoner teaches that leukotriene receptor antagonists (LTRAs) have been proven to be

effective as a primary, controller therapy, and add-on therapy with established efficacy, good safety profiles, and simple oral dosing requirements (page 390).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to at the time of invention was made to include administration of one more therapy such as leukotriene receptor antagonists (LTRAs) because Skoner teaches that LTRAs in combination to another asthma therapy are more efficacious, anti-inflammatory, and have good safety profiles when administered to a human child. One would have been motivated to administer IL-9 antagonists and one more asthma therapy such as LTRAs because Skoner teaches LTRAs (such as Zafirlukast and Montelukast) work well in controlling asthma and works when added-on to another asthma therapy. Further, Skoner teaches that the LTRAs are safe and efficacious in children (page 390). Additionally, one would have a reasonable expectation of success because Skoner teaches using LTRAs in combination to another therapy for controlling asthma in children.

Claims 9, 10, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levitt et al. (2001) in view Elliott, Michael (Phil. R. Soc. Lond. 356: 1885-1893, 2001).

Claims 9, 10, 29 and 30 are further drawn to a method of treating or ameliorating a respiratory infection or a symptom thereof in a human subject suffering therefrom, said method comprising administering an effective amount of an IL-9 antagonist wherein the respiratory infection is an influenza virus infection.

The teachings of Levitt et al are summarized as set forth supra. Levitt et al do not teach treating respiratory infection associated with influenza virus.

Elliott teaches that influenza is highly contagious respiratory tract infection that is caused by influenza type A and B viruses. They teach treating respiratory infection caused by influenza virus by administering a neuraminidase inhibitor known as Zanamivir (page 1885). Elliott teaches that the intranasal administration of zanamivir in humans infected with influenza virus reduces influenza related complications 17-31% compare with placebo (page 1889).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to at the time of invention was made to include administration of a neuraminidase inhibitor such as zanamivir in combination with an anti-IL-9 antagonist in a patient having respiratory infection associated with influenza virus. One would have been motivated to administer a therapy such as zanamivir that inhibits viral infection in combination with an IL-9 antagonist that reduces respiratory infection, asthma or an allergy because Elliott teaches that neuraminidase inhibitors significantly reduce influenza associated symptoms (abstract and page 1892). Further, one would have a reasonable expectation of success because, according to Elliott, a therapy like zanamivir has been clinically shown to reduce influenza associated complications in humans in clinical trials.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gyan Chandra, Ph.D.
Art Unit 1646
11 April 2007
Fax: 571-273-2922

GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600